should be compared with G-CSF mobilized peripheral blood stem cell collection.

Table. *Summary of Serious Marrow Complications*

→ Symptom Nature/ Duration ↓ Proximal Cause	Acute/ Atypical	Acute/ Known	Cancer	Herniated Disk	Prolonged Recovery/ Mild	Prolonged Recovery/ Moderate-Severe	Total
Anesthesia	15 (75%)	28 (97%)	0	0	2 (7%)	0	45 (36%)
Infection	1 (5%)	0	0	0	0	0	1 (1%)
Mechanical Injury	4 (20%)	0	0	0	25 (93%)	40 (100%)	69 (55%)
Unrelated/ Other	0	1 (3%)	6 (100%)	3 (100%)	0	0	10 (8%)
Total	20	29	6	3	27	40	125

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NEUTROPENIA AND THROMBOCYTOPENIA INDUCED BY G-CSF ADMINISTRATION IN HEALTHY PBSC ALLOGENEIC DONORS: HOW LONG SHOULD BE PROLONGED HEMATOLOGICAL AND CLINICAL SURVEILLANCE?

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From February 1998, one hundred and twenty peripheral blood stem cell (PBSC) healthy donors were treated with G-CSF for 4-7 days and submitted to leukoapheresis courses in the Apheresis Unit of our Service. All were enrolled on short and long-term clinical and hematological surveillance protocol for a five year time. To-date, 95 donors are evaluable: overall mean follow-up time is 31 months, being ≥36 months in 45 and <12 months in 13 subjects. Main clinical adverse effects to Lenograstim were headhache (65%), musculo-skeletal pain (78%) and fatigue (69%); no therapy or low paracetamol doses were employed in 95% of the donors. Pre-leukoapheresis mean platelet reduction was assessed at 23.6% ± 9% and detected in 42/95 cases; an additional decrease of absolute WBC counts, in particular due to both PMN and Lymphocyte low numbers, was diagnosed in 27 subjects of this group. Pre-G-CSF administration platelet values were observed at +12 months of follow-up. Multivariate and univariate analysis demonstrated a correlation between duration of G-CSF administration (p.004), pre G-CSF platelet level (p.003) and decreased platelet count before leukoapheresis. At this regard, PMN and or lymphocyte lower values were counted in 75 out of 95 donors two weeks after G-CSF administration, whereas PMN and Lymphocytes were significantly decreased in 43 out of the 75 subjects (-39.3% and -30%, respectively). Transient PMN count below 1000/ul was detected in 4/43 cases. Finally, in 12/43 donors pre mobilization number of PMNs or Lymphocytes were reached only after 24 months of follow-up time. Univariate and multivariate analysis demonstrated strict correlation between-n reduction at +4, +8, and +12 months of follow-up, and G-CSF administration days (p.0021) + pre-mobilization PMN absolute counts (p.003). Sex and age of patients did not significantly correlate with WBC decremental trend; however, isolated PMN low values were more frequently observed in young patients, since in this group mean age was 38.5 ± 15 yrs in comparison to lymphocytopenic donors (44.7 ± 5 yrs). Taken altogether, these results seem to demonstrate in younger PBSC donors treated with G-CSF for more than five days, negative effects on myelopoiesis lasting two years, without any findings of haematological disorders or clinical sign of disease. In these limited cases, a hematocromocytometric observation may be prudentially prolonged over five years.

Table. *Variation of PMN in 24 Months of Follow-up Time*

	T0 PMN counts	% Decrement + 14	% Decrement + 4m	% Decrement + 8m	% Decrement + 12m	% Decrement + 24m
10 Patients lymphopenic	3310 ± 320	not change	not change	not change	not change	not change
22 Patients neutropenic	4450 ± 1220	37.5 ± 13.9	12 ± 5	8 ± 3	9 ± 3.5	12.4 ± 4
43 Patients ly + neutropenic ±	3855 ± 456	39.5 ± 14	15 ± 3.7	10 ± 2.8	13 ± 6	21.6 ± 9

AUTOLOGOUS

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PEGFILGRASTIM (NEULASTA™) FOLLOWING CHEMOTHERAPY LEADS TO SUCCESSFUL MOBILIZATION OF HEMATOPOIETIC PROGENITOR CELLS AMONG TRANSPLANT PATIENTS WITH VARIOUS DIAGNOSES

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Filgrastim has been traditionally used following chemotherapy to mobilize hematopoietic progenitor cells. Doses of 5-10 μg/kg/day subcutaneously have been given until recovery of WBC counts to over $5.0 \times 10^3/\mu L$ before initiating leukapheresis. Pegfilgrastim (Neulasta™) produced by covalently binding a 20-kd monomethoxypolyethylene glycol molecule to the N-terminal methionyl residue of filgrastim has a much longer half-life allowing for a single 6 mg subcutaneous injection with similar efficacy and safety profile as filgrastim in reducing the duration of severe chemotherapy-induced neutropenia. Thirteen patients with various diagnoses (6 Myeloma, 4 NHL, 1 breast cancer, 1 seminoma, 1 CLL) received pegfilgrastim 6 mg single injection 1 day after completing mobilization chemotherapy (cytoxan+etoposide = 8; cytoxan = 2; ICE ± Rituximab = 2; taxotere+adriamycin+cytoxan = 1). The median age was 56 years (28-71) with 8 females and 5 males. Leukapheresis processing 3 times the estimated blood volume was initiated beginning recovery of total WBC count to at least $5.0 \times 10^3/\mu L$. The minimum target of 2.5×10^6/kg CD34+ cell count was achieved 100% in all 13 patients after only one day of leukapheresis. The optimal target of 5.0×10^6/kg CD 34+ cell count was obtained in 85% (11/13 patients) in a single day of collection. The mean CD34+ cell count collected in the first day was 16.8×10^6/kg (median 13.6, range 2.5 – 45.5). Two patients (1 CLL, 1 Myeloma with CLL) had their harvested product CD34-selected before cryopreservation. All patients engrafted following their autotransplants. Engraftment data were as predicted for peripheral blood stem cell recovery times (Time to ANC of >500/μL: mean 10.3 days, range 8-11 and time to Platelet count $>20 \times 10^3/\mu L$: mean 11.5 days, range 9-15). In conclusion, pegfilgrastim given as a single 6 mg subcutaneous injection after chemotherapy is a viable alternative to multiple daily injections of filgrastim for the mobilization of hematopoiteic progenitor cells.

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PERIPHERAL BLOOD STEM CELL TRANSPLANT (PBSCT) IN A LARGE SERIES OF PATIENTS WITH POEMS SYNDROME

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Background: The POEMS syndrome is characterized by peripheral neuropathy (PN), clonal plasma cell disorder (PCD), organomegaly, endocrinopathy, skin changes, edema, sclerotic bone lesions, and thrombocytosis. Based on the improved response rates observed with PBSCT in patients with other PCD, autologous

PBSCT may be an attractive treatment option for patients with POEMS syndrome. **Methods:** Between March 1999 and February 2003, 11 patients with POEMS syndrome underwent PBSCT at Mayo Clinic Rochester and Jacksonville. Conditioning regimens were single agent melphalan (n = 9) and BEAM (n = 1). All received a minimum of 4.4×10^6 CD34 autologous PBSC/kg. Standard supportive care with prophylactic antibiotics and growth factor support was provided. **Results:** All but one had a severe rapidly progressive sensorimotor PN involving both upper and lower extremities, 7 wheelchair confined. One patient had sensory neuropathy without significant motor involvement. All but one was male. A monoclonal lambda PCD was documented in all patients, and two had biopsy proven Castleman Disease. Median age was 50 years (range 19-62). Seven had organomegaly (5 splenomegaly; 2 hepatomegaly; and 3 lymphadenopathy). Both endocrinopathy and skin changes were present in 9 patients. Seven had thrombocytosis and/or erythrocytosis, and 8 had sclerotic bone lesions (diffuse in 5, solitary lesion in 3). Using the Bardwick Criteria, the median number of POEMS features was 5 (range 2-5). The median number of therapeutic regimens prior to PBSCT was 3 (range 0-6). From first symptoms and from diagnosis of POEMS the median times to transplant were 27 and 10 months (ranges 4-180 and 2-180), respectively. All but one patient had significantly abnormal pre-transplant pulmonary function tests. Of the 8 evaluable patients, all have had a hematologic response and 7 have had neurologic improvement at a median follow-up of 6 months. Other symptoms including fatigue, organomegaly, pulmonary compromise, hyperpigmentation and extravascular volume overload have improved substantially in affected patients. Since February 2003, an additional 4 patients have been transplanted, but are not yet evaluable. **Conclusions:** PBSCT for POEMS syndrome may result in a high hematologic response rate and improvement in peripheral neuropathy and systemic symptoms. The outcome of these patients will be updated at the meeting.

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GASTROINTESTINAL GRAFT-VERSUS-HOST DISEASE AFTER AUTOLOGOUS STEM CELL TRANSPLANT: INCIDENCE, OUTCOME, AND RISK FACTORS

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GVHD has been described in the skin, intestinal mucosa, and liver after autologous stem cell transplantation. The mechanisms and risk factors for non-cyclosporine-induced autologous GVHD are unknown. **Methods:** We reviewed 681 consecutive autologous transplant patients treated between 1995–1999 to determine the incidence of response to treatment, and risk factors for developing gastrointestinal GVHD. GVHD was defined by persistent symptoms, mucosal abnormalities at endoscopy, histology showing apoptotic crypt-cells and lymphoid infiltrates, and absence of infection. **Results:** The incidence of GVHD was 90/681 (13%), with nausea, vomiting, and anorexia in 90% and diarrhea in 37%. The mean time to onset was day + 15 and endoscopic diagnosis day + 45. Treatment with prednisone (1 mg/kg/d) for 10-14 days followed by a taper effected durable responses in 72%; an additional 19% responded to a second course. GVHD developed in 18% of the women and 8% of the men. Significant risk factors in univariate analysis included female sex (p = .0009), diagnosis of breast cancer (BRCA) (p = .0001), IL-2 therapy (p = .04), Busulfan/Melphalan/Thiotepa (BUMELTT) conditioning (p = .03) and use of PBSC (p = .025). All cases of GVHD were in patients who received PBSCs. Females with BRCA were 3.3x more likely to develop GVHD than males with any diagnosis (95% C.I., 1.9-5.8, p < .0001). Gravidity and parity of females did not statistically affect the risk for developing GVHD. Since women were more likely to receive BUMELTT conditioning, the data was analyzed adjusting for this regimen. A multivariate logistic regression model revealed the following: (see Table 1)

The hazard of mortality (or relapse) of patients with GVHD compared to those without was not significantly different for the cohort as a whole nor across different genders/diagnoses (HR: 0.89, 95% C.I. 0.64-1.22, p = .46). **Conclusions:** Gastrointestinal GVHD developed in 13% of 681 autologous transplant recipients and was responsive to short courses of prednisone. Female sex appears to be the most important risk factor. Although BUMELTT appears to increase the odds of developing GVHD, female gender and underlying disease carried an increased risk for developing GVHD independent of the conditioning regimen.

Table.

Gender/diagnosis	O.R.	95% C.I.	*P* Value
Male/lymphoma, myeloma, or hem. malignancy	1	—	—
Female/BRCA	3.4	1.8-6.6	.0002
Female/lymphoma, myeloma, or hem. malignancy	2.9	1.4-6.0	.003
Male/other diagnoses	3.0	1.2-7.5	.02
Female/other diagnoses	2.2	0.9-5.5	.08

GRAFT PROCESSING

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SIGNIFICANCE OF LOW PERIPHERAL BLOOD CD34+ CELL NUMBERS PRIOR TO LEUKAPHERESIS: SHOULD THE 5/μL THRESHOLD REQUIRED FOR APHERESIS BE CHANGED?

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The pre-apheresis peripheral blood CD34+ cell count (PBCD34) is a strong predictor of the CD34+ cell collection. The final yield is also affected by the blood volume processed and the CD34+ cell collection efficiency (CE). It is common practice to apherese only when PBCD34 is 5/μL to avoid poor yields. However, many patients mobilize stem cells poorly, and the only way to get enough cells is to collect small numbers at a time over several days. Omitting apheresis because PBCD34 is below a set value may prevent them from undergoing a transplant. There are other pitfalls with this practice: it does not take the patient's weight into account, and it ignores the possibility of improving the collection by processing more blood. Of 485 autologous harvests on Cobe Spectra over 30 months where PBCD34 was available, 104 were done with PBCD34 <5/μL. Volume processed was 15 L (n = 57) or 20 L (n = 47). A collection of $\geq 0.3 \times 10^6$ CD34+ cells/kg was considered acceptable as this daily yield over a week could add up to 2×10^6/kg-enough for an autograft. 60 harvests (58%) had yields of ≥0.3; with 49% being ≥0.4, 38% being ≥0.5 and 23% being ≥0.6. CE for these 104 harvests was 9-145% (median 55%) compared to 7-132% (median 45%) for the other 381 harvests performed with PBCD34 ≥5/μL (P = 0.0001). CE for the 60 harvests with CD34+ yields ≥0.3 was 30-145% (median 70) compared with 9-118% (median 35%) for the 44 with CD34+ yields <0.3 (P < 0.0001). This suggests that part of the reason for poor collection was low CE in addition to poor mobilization. The problem of low CE may be solved in part by using more experienced operators if the mononuclear cell protocol is used for apheresis or using an automated collection protocol such as AutoPBSC. These data show that an arbitrary PBCD34 threshold of 5/μL is inappropriate to deny apheresis. We suggest using the following formula for patients with PBCD34 <5/μL to decide about appropriateness of apheresis: 14n/w; where n = PBCD34/μL and w = ideal body weight in kg. A 20 L apheresis with 70% CE is assumed ($20 \times 0.7 = 14$). If 14n/w is ≥0.3, apheresis should be performed. This approach is more logical than using an absolute threshold, and ensures that patients are not deprived of the opportunity of stem cell collection and autotransplantation. We conclude that it is clinically inappropriate to set an arbitrary minimum PBCD34 threshold for apheresis. This practice